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EXAMINER	
BERCH, MARK L	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 09/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/608,689	BIGOT ET AL.	
	Examiner	Art Unit	
	Mark L. Berch	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/21/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 2-5, 7-8 drawn to W=N or N→O, classified in class 544; 536, subclass 118,277; 27.3,27.62.

II. Claims (none), drawn to W=C, classified in class 546; 536, subclass 118; 27.13.

Claims 1, 6 and 9-14 link inventions I and II. These claims are examined to the extent that they read on the elected invention.

The inventions are distinct, each from the other because of the following reasons:

The two cores provide different heterocyclic ring systems. Group I constitutes purines. Group II constitutes imidazopyridines. These different in the number of heteroatoms present in the heterocyclic core.

Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

During a telephone conversation with Barbara Kurys on 7/25/2006 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-14. Affirmation of this election must be made by applicant in replying to this Office action. Claim (none) are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1, 6 and 9-14 are rejected as being drawn to an improper Markush Group. The claims are drawn to multiple inventions for reasons set forth in the above requirement

for restriction. This does not constitute an art recognized genus. Because of the marked structural differences at a part of the molecule essential for utility, the claims are deemed to lack unity of invention (see *In re Harnish*, 206 USPQ 300). The claims are examined only to the extent that they read on the elected invention. Cancellation of the non-elected subject matter (W=C) will overcome the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6-7 are rejected under 35 U.S.C. 102(b) as being anticipated by WO99/24450.

Intermediate 5 anticipates. It avoids the last proviso because it does not have A and B as OH but as acetoxy, which is permitted by the definition of R' and R".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6-7, 9-14are rejected under 35 U.S.C. 103(a) as being unpatentable over WO99/24450.

See the last species on page 5. This is the species excluded by the third proviso. However, the position homolog, i.e. the compound bound at the 2- or 3-position of the pyridyl, or the

compound where the pyridyl is at the 1-position of the ethyl, is not excluded by the proviso and hence would be rendered obvious by this species. It is well established that position isomers are prima facie structurally obvious even in the absence of a teaching to modify. The isomer is expected to be preparable by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing the position isomers. This circumstance has arisen many times. See: *Ex parte Englehardt,* 208 USPQ 343, 349; *In re Mehta,* 146 USPQ 284, 287; *In re Surrey,* 138 USPQ 67; *Ex Parte Ullyot,* 103 USPQ 185; *In re Norris,* 84 USPQ 459; *Ex Parte Naito,* 168 USPQ 437, 439; *Ex parte Allais,* 152 USPQ 66; *In re Wilder,* 166 USPQ 545, 548; *Ex parte Henkel,* 130 USPQ 474; *Ex parte Biel,* 124 USPQ 109; *In re Petrzilka,* 165 USPQ 327; *In re Crownse,* 150 USPQ 554; *In re Fouche,* 169 USPQ 431; *Ex parte Ruddy,* 121 USPQ 427; *In re Wiechert,* 152 USPQ 247, *In re Shetty,* 195 USPQ 753; *In re Jones,* 74 USPQ 152, 154.

For example, "Position isomerism has been used as a tool to obtain new and useful drugs" (Englehardt) and "Position isomerism is a fact of close structural similarity" (Mehta, emphasis in the original). Note also *In re Jones,* 21 USPQ2d 1942, which states at 1943 "Particular types or categories of structural similarity without more, have, in past cases, given rise to *prima facie* obviousness"; one of those listed is "adjacent homologues and structural isomers". Position isomers are the basic form of close "structural isomers." Similar is *In re Schechter and LaForge,* 98 USPQ 144, 150, which states "a novel useful chemical compound which is homologous or isomeric with compounds of the prior art is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compounds." Note also *In re Deuel* 34 USPQ2d 1210, 1214 which states, "Structural relationships may provide the requisite motivation or suggestion to

modify known compounds to obtain new compounds ... a known compound may suggest its analogs or isomers, either geometric isomers (cis v. trans) or position isomers (e.g., ortho v. para)." See also MPEP 2144.09, second paragraph.

Second, the species would render obvious the chain homolog, i.e. where the pyridyl is attached to the terminal carbon of a propyl, or to a methyl group. Compounds that differ only by the presence or absence of an extra methyl group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologue. As was stated in *In re Grose*, 201 USPQ 57, 63, "The known structural relationship between adjacent homologues, for example, supplies a chemical theory upon which a prima facie case of obviousness of a compound may rest." The homologue is expected to be preparable by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methyl groups. See *In re Wood*, 199 USPQ 137; *In re Hoke*, 195 USPQ 148; *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 247; *Ex parte Henkel*, 130 USPQ 474; *In re Jones*, 74 USPQ 152, 154; *In re Herr*, 134 USPQ 176; *Ex parte Dibella*, 157 USPQ 59; *In re Zickendraht*, 138 USPQ 22; *Ex Parte Fischer*, 96 USPQ 345; *In re Fauque*, 121 USPQ 425; *In re Druey*, 138 USPQ 39; *In re Bowers and Orr*, 149 USPQ 570. In all of these cases, the close structural similarity between two compounds differing by one or two methyl groups was itself sufficient show obviousness. As was stated directly in THE GENERAL TIRE & RUBBER COMPANY v. JEFFERSON CHEMICAL COMPANY, INC., 182 USPQ 70 (1974): "If any structural

change is obvious to one skilled in the art, a substitution of the next higher homolog would seem to be." Note also *In re Jones*, 21 USPQ2d 1942, which states at 1943 "Particular types or categories of structural similarity without more, have, in past cases, given rise to *prima facie* obviousness"; one of those listed is "adjacent homologues and structural isomers". Similar is *In re Schechter and LaForge*, 98 USPQ 144, 150, which states "a novel useful chemical compound which is homologous or isomeric with compounds of the prior art is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compounds." Note also *In re Deuel* 34 USPQ2d 1210, 1214 which states, "Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties." See also MPEP 2144.09, second paragraph.

Third, it would render obvious a compound having an extra methyl, attached to either the ethyl chain or the pyridyl. Compounds that differ only by the presence or absence of an extra methyl group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologue. As was stated in *In re Grose*, 201 USPQ 57, 63, "The known structural relationship between adjacent homologues, for example, supplies a chemical theory upon which a prima facie case of obviousness of a compound may rest." The homologue is expected to be preparable by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious

even in the absence of a specific teaching to add or remove methyl groups. See *In re Wood*, 199 USPQ 137; *In re Hoke*, 195 USPQ 148; *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 247; *Ex parte Henkel*, 130 USPQ 474; *In re Jones*, 74 USPQ 152, 154; *In re Herr*, 134 USPQ 176; *Ex parte Dibella*, 157 USPQ 59; *In re Zickendraht*, 138 USPQ 22; *Ex Parte Fischer*, 96 USPQ 345; *In re Fauque*, 121 USPQ 425; *In re Druey*, 138 USPQ 39; *In re Bowers and Orr*, 149 USPQ 570. In all of these cases, the close structural similarity between two compounds differing by one or two methyl groups was itself sufficient show obviousness. As was stated directly in THE GENERAL TIRE & RUBBER COMPANY v. JEFFERSON CHEMICAL COMPANY, INC., 182 USPQ 70 (1974): "If any structural change is obvious to one skilled in the art, a substitution of the next higher homolog would seem to be." Note also *In re Jones*, 21 USPQ2d 1942, which states at 1943 "Particular types or categories of structural similarity without more, have, in past cases, given rise to *prima facie* obviousness"; one of those listed is "adjacent homologues and structural isomers". Similar is *In re Schechter and LaForge*, 98 USPQ 144, 150, which states "a novel useful chemical compound which is homologous or isomeric with compounds of the prior art is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compounds." Note also *In re Deuel* 34 USPQ2d 1210, 1214 which states, "Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties." See also MPEP 2144.09, second paragraph.

Finally, that species would render obvious the corresponding trifluoroethyl analog. Note that the reference says that R3 is fluoroalkyl generally, and the trifluoroethyl choice is seen in the last 4 species of the page 6 list, and hence is an ovious variation. Such a species would avoid the proviso as well.

With regard to claims 6 and 7, Intermediate 6 is excluded by the last proviso. However, since the 6-Cl is a leaving group, other halogens would be obvious to one of ordinary skill in the art of organic synthetic chemistry as leaving groups.

As for claims 9-14, the utility is the same.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 6-7, 9-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. The term "pseudohalogen" is indefinite. This is a loose term; it does not have a single generally accepted definition. Are the fulminate ion (ONC^-), cyanamide ion (NCN^{2-}), azide dithiocarbonate ion ($SCSN_3^-$) included? These sometimes occur as examples of

pseudohalogens, but generally do not. The specification gives only two "examples", so the full scope cannot be deermined.

2. The term "general formula" is indefinite. A formula cannot be both general and specific; deletion is suggested.
3. The "functionalization" of the last line of claim 13 is of unknown meaning. Its scope is unclear.
4. The use of "Y-X" in the provisos is not correct and is confusing. Y is already and always part of X. The substituent on the 6-position of adenine is X, not –X-Y. Y is not a substituent which is attached to X, Y is part of X.
5. Reference to C1 alkenyl is the X definition, and in the last proviso are wrong, as alkenyl must have at elast 2 carbons.
6. The last term in claim 1 appears to be forbidden. It is a methyl substituted by cycloalkyl. However, cycloalkyl is not a permitted substituent on X=alkyl, nor is it a permitted choice for Y itself.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for other forms, does not reasonably provide enablement for solvates and hydrates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims, insofar as they embrace solvates and hydrates are not enabled. The numerous examples presented all failed to produce a solvate. The evidence of the specification is thus clear: These compounds do not possess the property of forming solvates; there is no evidence that such compounds even exist. These cannot be simply

willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist." The same circumstance appears to be true here: there is no evidence that solvates or hydrates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that solvates can be made, or limit the claims accordingly.

Claims 9 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for first two and the last listed, does not reasonably provide enablement for the other three. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.
The analysis is as follows:

(1) Breadth of claims.

(a) Scope of the compounds. Because of the broad scope of the primary variables X, A, B and T, trillions of compounds are covered.

(b) Scope of the diseases covered.

A. Cardiovascular. Cardiovascular disorders embraces a vast array of problems, some of which are contradictory to others. This covers various forms of endocarditis, including Verrucous, Atypical verrucous (Libman-Sacks) Non-bacterial thrombotic - NBTE (marantic), bacterial, viral, and rickettsial endocarditis. It covers different forms of atresia, including tricuspid atresia without TGV, pulmonic valvular atresia and aortic atresia. It includes assorted cardiomyopathies, including restrictive cardiomyopathy, peripartum cardiomyopathy, hypertrophic cardiomyopathy, and congenital cardiomyopathy. It embraces various forms of aortic Stenosis, including valvular aortic Stenosis, idiopathic hypertrophic sub-aortic stenosis (IHSS), subvalvular aortic stenosis, and supravalvular aortic stenosis. There are all kinds of miscellaneous syndromes, including subclavian steal syndrome, Eisenmenger syndrome, mitral valve prolapse (Barlow) syndrome, Aortic arch syndrome, scimitar syndrome, hypoplastic left heart syndrome, Lutembacher syndrome, and superior vena cava syndrome. It covers various forms of hypertension, including primary (idiopathic) pulmonary hypertension, neonatal pulmonary venous hypertension and pulmonary hypertension. It includes aortic aneurysms, including both thoracic and abdominal, as well as mycotic aneurysm. It covers various types of arrhythmias and atrial fibrillation. It covers elevated blood levels of triglycerides, of total cholesterol or of LDL cholesterol, and hyperlipoproteinaemias. It covers different forms of ischaemic heart disease including congestive heart failure and myocardial infarction. It covers a vast array of structural defects such as atrial septal

defect (ASD), aorticopulmonary window, egg-on-its-side heart, gooseneck deformity, endocardial cushion defect, arc of Buehler, arc of Riolan, truncus arteriosus, Ebstein's Malformation, azygos continuation of interrupted IVC, Atrioventricular Canal, ventricular septal defect (VSD), abdominal aortic coarctation, aortic pseudo-coarctation, complete endocardial cushion defect, Hypoplastic Left Heart, patent ductus arteriosus (PDA), congenital absence of pulmonary valve, aortic coarctation partial endocardial cushion defect, Single Ventricle, box-like heart, pulmonary sling, Left Ventricle to Right Atrial Shunt, total anomalous pulmonary venous return (TAPVR), partial anomalous pulmonary venous return (PAPVR), and transposition of the great vessels. It covers certain peripheral vascular disorders, such as deep-vein thrombosis and thrombophlebitis and assorted cerebral vascular diseases including migraine. There is hypotension, which can arise from all sorts of other problems. There are a number of different forms of vasculitis, including Churg-Strauss vasculitis, consecutive vasculitis, granulomatous vasculitis of central nervous system, hypersensitivity vasculitis, (called also allergic or leukocytoclastic vasculitis or leukocytoclastic angiitis which arises from hypersensitivity to an antigenic stimulus), hypocomplementemic vasculitis, isolated vasculitis of central nervous system, nodular vasculitis, overlap vasculitis (polyangiitis overlap syndrome), pulmonary vasculitis including Wegener's granulomatosis, rheumatoid vasculitis, segmented hyalinizing vasculitis (livedo vasculitis), Polyarteritis nodosa, and urticarial vasculitis. There are also specific forms of arteritis, including coronary arteritis, equine viral arteritis, giant cell arteritis (cranial, granulomatous, or temporal arteritis or Horton's disease), infantile arteritis, infectious arteritis, arteritis obliterans (endarteritis obliterans), rheumatic arteritis, syphilitic arteritis, Takayasu's arteritis (aortic arch, or brachiocephalic arteritis

or Martorell's syndrome or pulseless disease), tuberculous arteritis, endarteritis obliterans, arteritis umbilicalis, and verminous mesenteric arteritis. There are different forms of Vascular dementia, including multi-infarct dementia (MID), Binswanger's Disease and Arteriosclerotic Dementia. There is a huge collection of other cardiovascular problems, including thymoma (invasive and non-invasive), admixture lesion, left ventricular hypertrophy, tortuous aorta, aortic laceration pulmonary artery sarcoma, aortic regurgitation, pneumomediastinum (Spontaneous and traumatic), middle mediastinal mass, posterior mediastinal mass, Uhl disease, right ventricular hypertrophy, cardiac rhabdomyoma, acute aortic dissection, pericardial cyst, carotid artery bruit, pulmonary embolism, venous angioma, varicose veins and spider veins, congenital heart disease, pericardial effusion, tetralogy of Fallot, coronary artery calcification, endocardial fibroelastosis, fibromuscular dysplasia (FMD), thromboangiitis obliterans (Buerger disease), left or right ventricular volume overload, situs inversus, neonatal heart failure, myocarditis, arteriosclerosis, atherosclerosis, stroke and many others.

B. Lipid disorders. Disorders of lipid metabolism covers a vast range of very different metabolic problems, These include Wolman's disease; Cerebrotendinous xanthomatosis (an accumulation of cholestanol); sitosterolemia, Refsum's disease (phytanic acid accumulates); Gaucher's disease, which occurs in three different forms (glucocerebrosides accumulate); Niemann-Pick (sphingomyelin accumulates), also in three different forms; Tay-Sachs disease (gangliosides accumulate), Fabry's disease (glycolipids accumulate); Farber disease (which accumulates ceramide); Krabbe Disease (which accumulates psychosine and galactoceramide); Metachromatic Leukodystrophy (sulfatide accumulates); Multiple Sulfatase deficiency (sulfatide and mucopolysaccharides accumulate); Galactosialidosis (no

storage product); GM2 gangliosidosis, which exists in three forms (accumulating GM2 ganglioside, GA2 and/or globoside, depending on which form); GM1 gangliosidosis (GM1 gangliosides, glocoproteins, oliosaccharides); Abetalipoproteinemia; hypobetalipoproteinemia; familial ligand-defective Apo-B; hepatic triglyceride lipase (HGTL) deficiency and Cholesterol ester transfer protein (CETP) deficiency. There is also Zellweger, Zellweger-like, Infantile Refsum's disease, adrenoleukodystrophy, and Rhizomelic Chondrodysplasia Punctata which are all peroxisome assembly disorders, although in most cases the primary deficit is unknown. There is also Acyl-CoA deficiency disorder; X-linked adrenoleukodystrophy; bifunctional enxyme deficiency, thiolase deficiency; dihydroxyacetone phosphate acyltransferase (DHAPAT) deficiency; pipecolic academia; Classical Refsum's disease (phytanic acid accumulates); glutaric aciduria Type III; and hyperoxaluria, which are all peroxisome function deficiencies. There are also infantile neuronal ceroid lipofuscinosis. (INCL) and late infantile neuronal ceroid lipofuscinosis (LINCL), both of which can occur in the Finish variant, which are neuronal ceroid lipofuscinoises. There are also Apo-deficiencies, which come in three types; familial lecithin-cholesterol acyltransferase deficiency and fish-eye disease; and Tangier Disease, all of which involve corneal clouding. There is also lipoprotein lipase deficiency; apolipoprotein C-II deficiency; familial dysbetalipoproteinemia, all of which can cause assorted Xanthomas. There is an entire constellation of fatty acid metabolism disorders. Some are Coenzyme A dehydrogenase deficiencies: Very long-chain acyl-coenzyme A dehydrogenase deficiency (VLCAD); Long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency (LCHAD); Medium-chain acyl-coenzyme A dehydrogenase deficiency (MCAD); Short-chain acyl-coenzyme A dehydrogenase deficiency (SCAD); and Short chain L-3-hydroxyacyl-coA

dehydrogenase deficiency (SCHAD). Other Coenzyme A enzyme deficiency disorders include 2,4 Dienoyl-CoA reductase deficiency; 3-hydroxy-3-methylglutaryl-CoA lyase deficiency; and Malonyl-CoA decarboxylase deficiency. The Carnitine related ones are Primary carnitine deficiency; Carnitine-acylcarnitine translocase deficiency; Carnitine palmitoyltransferase I deficiency (CPT); and Carnitine palmitoyltransferase II deficiency (CPT). There are also some miscellaneous one, including Mitochondrial trifunctional protein deficiency; Electron transfer flavoprotein (ETF) dehydrogenase deficiency (also known as GAII or MADD).

C. Metabolic Syndrome. Metabolic Syndrome (also known as Syndrome X; Metabolic syndrome X; Reaven's Syndrome and abdominal obesity-metabolic syndrome) is a clustering of abdominal obesity, high triglycerides, low levels of high density lipoprotein cholesterol (HDLC), high blood pressure, and elevated fasting glucose levels.

(2) The nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(3) Direction or Guidance: That provided is very limited. The daily dosage range information on page 22 is completely generic, not specific for this or that disease.

(4) State of the Prior Art: The compounds are adenines with a particular set of saturated heterocycles attached to the exocyclic N, and a particular substitution patter and the 9-position. So far as the examiner is aware, no adenines with any heterocycles attached to the exocyclic N are in use for such disorders.

(5) Working Examples: There are no working examples for any of these disorders.

(6) Skill of those in the art:

A. The skill level in the art of pharmacological treatment of cardiovascular disorders varies with the disorder. In some areas such as hypertension it is relatively high. But in the great majority of cases it is very low as the disorders cannot be treated with pharmaceuticals. There are a wide variety of causes. For example, just for the Vascular dementias, these can be caused when caused when small arteries in the brain burst (cerebral hemorrhage), or arteries are blocked by plaque formation or clots (thrombosis or embolism), or there is insufficient blood flow to parts of the brain (ischemia). Stroke is the most common cause, but it can arise from auto-immune inflammatory diseases of the arteries such as Systemic Lupus Erythermotsis and Temporal Arteritis; sometimes the cause is completely unknown. A huge assortment of inflammatory processes can result in various forms of vasculitis. Genetic defects and developmental problems are responsible for many types of structural problems. Metabolic disorders such as Mucopolysaccharidosis I (the cause of Hurler- Scheie syndrome) can cause vascular deposits of mucopolysaccharides with arteriosclerosis, heart murmur, and aortic regurgitation. The vast majority are treated either by surgical means or cannot be treated at all, leaving only general management of symptoms.

B. The etiology for Metaolic Syndrome remains unknown, and there is no treatment for the disorder per se. The predominant approach is non-pharmaceutical, viz., caloric restriction and physical activity. If treated with drugs, the individual manifestations that comprise the metabolic syndrome are treated separately, e.g. diuretics and ACE inhibitors for hypertension; cholesterol drugs to lower LDL cholesterol and triglyceride levels as needed.

Use of drugs that decrease insulin resistance e.g. metformin and thiazolidinediones is controversial and has not been established as effective.

C. Lipid disorders vary according to the nature of the storage product (if any), the measured deficiency (which isn't always known), and the genetic defect responsible (which is sometimes also not known). The great majority are totally untreatable per se, and for many even palliative measures are limited or unavailable, and some are fatal in very short order. The notion that any compound could treat these generally is completely inconsistent with the wide range of storage products, enzyme deficiencies and genetic defects involved.

(7) The quantity of experimentation needed: Owing especially to factors (1) and (6), the quantity of experimentation is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claim Objections

The last two choices for aryl in claim 2 are misspelled.

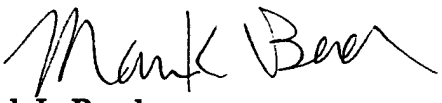
Specification

The abstract is objected to as vague. A definition for X is needed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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9/1/2006